REMARKS

This is a Divisional Application of application Serial No. 09/167,151.

In the March 7, 2000 Office Action in parent application Serial No. 09/167,151, there was a Restriction Requirement under 35 USC 121 involving Groups I to IV. Group I was elected in response to said Restriction Requirement in application Serial No. 09/167,151. The clams in this Divisional application are directed to the claims of non-elected Groups II to IV.

The specification was editorially revised.

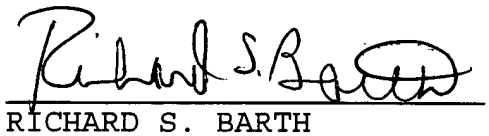
A MARKED UP VERSION OF THE AMENDMENTS TO THE SPECIFICATION is enclosed.

Also enclosed is a MARKED UP VERSION OF THE AMENDED CLAIMS.

New claims 89 and 90 contain features of original claim 62.

Enclosed is a copy of the DECLARATION UNDER 37 CFR 1.132 of Dr. Tohru TAKAHASHI, dated December 15, 1997, the original of which was filed in grandparent application Serial No. 08/500,635.

Respectfully submitted,



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Enclosures: (1) Replacement specification pages 127 to 140 of the Sequence Listing

(2) MARKED UP VERSION OF THE AMENDMENTS TO THE SPECIFICATION

(3) MARKED UP VERSION OF THE AMENDED CLAIMS

(4) Copy of DECLARATION UNDER 37 CFR 1.132 of Dr. Tohru TAKAHASHI, dated December 15, 1997

MARKED UP VERSION OF THE
AMENDMENTS TO THE SPECIFICATION

Paragraph bridging pages 12 and 13:

--The present invention will be illustrated with respect to the accompanying drawings, in which:

Figure 1 is a restriction enzyme map of cDNA of the NIa region isolated from CYVV-cDNA;

Figure 2 is a schematic drawing which shows the construction of plasmid pKNI5' containing a 5'-region of NIa;

Figure 3 is a schematic diagram which shows the construction of plasmid pKNI5IL containing a part of the IL-11 gene and a 5'-region of NIa;

Figure 4 is a schematic diagram which shows primers which were used to prepare the 5'IL DNA fragment, the CIN3 DNA fragment and in which the 3'-terminus of the NIa gene and the 5'-terminus of the IL-11 gene are fused;

Figure 5 is a schematic diagram which shows the fusion of the CIN3 DNA fragment and the [IL5'DNA] 5'IL DNA fragment by PCR;

Figure 6 is a schematic diagram which shows the construction of plasmid pKSUN9;

Figure 7 is a construction enzyme map of pUCKM31-7;

Figure 8 is a comparative diagram of the nucleotide sequences of the 3' terminals in pUCKM31-7 and pcD-31;

Figure 9 is a construction diagram of [pSR α31-7] pSRα31-7;

Figure 10 is a schematic diagram [of] showing the introduction of a histidine hexamer encoding sequence into pUCKM31-7;

Figure 11 is a construction diagram [of] for pMAL31-7;

[Figure 12 is a diagram] Figures 12A and 12B are graphs showing the results of the assay of dichlorophenol-indophenol reducing activity; and

Figure 13 is a graph showing the determination of oxidized glutathione reducing activity.--

Paragraph bridging pag s 99 and 100:

--The next step was to verify that the several specific 60 kDa bands identified in Example 11 are the same as the polypeptide encoded by the insert of pSRα31-7. It was also desired to determine the N-terminal amino acid sequence of this polypeptide. Accordingly, a clone was prepared wherein an extra six His residues were encoded for the C-terminal of the polypeptide before te step codon. Histidine residues have a high affinity for Ni^{2+} and the objective was to express a polypeptide having a histidine hexomer (6 x His), which could be purified using an affinity resin column charged with [NI^{2+}] $\underline{Ni^{2+}}$.--

Paragraph bridging pages 105 and 106:

--90.4 µg, as determined using the Protein Assay Kit (Bio-Rad), of each of the chromatography samples obtained in ii) above were separately mixed with 1 ml of 50 µM DCIP (Sigma). 15 µl of 1 mM NADPH (Boehringer-Mannheim) were then added to each of the samples and the OD_{600nm} and OD_{340nm} absorbance values were monitored with time. The resulting decrease in absorbance at both wavelengths [as] <u>is</u> shown in [Figure 12] <u>Figures 12A and 12B,</u> and it can be seen that only the pMAL31-7 sample contains a factor that reduces DCIP.--

Page 115, last paragraph:

--The resulting sediment was suspended in SDS-PAGE sample buffer [sulution] solution containing 10 μl of 2-mercaptoethanol. Each suspension was heated at 90°C for 2 minutes, and then SDS-PAGE was performed under reducing conditions using a 12.5% gel. Following electrophoresis, the product was transferred from polyacrylamide gel to a nitrocellulose film (BIO-RAD). Western blotting was performed using the polyclonal anti-KM31-7 antibody described in Example 1, part (a) and the anti-KM31-7 monoclonal antibody was determined to specifically precipitate KM31-7 protein from COS-1/pSRα31-7 serum-free culture supernatant.--

MARKED UP VERSION OF THE AMENDED CLAIMS

48. (Amended) A polypeptide having the sequence [given by] consisting essentially of residue numbers 4 to 437 in [sequence] SEQ ID [number] NO:2 [in the sequence listing].

55. (Amended) [The] A polypeptide [encoded by the polynucleotide sequence of claim 49] which consists essentially of amino acid numbers 1 to 526 of SEQ ID NO: 12, and which catalyzes the reduction of dichloroindophenol and oxidized glutathione.

60. (Amended) [The] A polypeptide [encoded by the polynucleotide sequence of claim 54] having the sequence consisting essentially of -23 to 526 of SEQ ID NO: 12.

61. (Amended) A method for the prophylaxis or treatment of conditions caused by, or related to, oxidative stress, or [any] a disease caused by activated oxygen, comprising [the administration] administering to a mammal in need thereof [an] a pharmaceutically effective, non-toxic dose of a peptide [encoded

by the polynucleotide sequence of claim 49] comprising the amino acid sequence consisting essentially of amino acid numbers 1 to 526 of SEQ ID NO: 12, and which catalyzes the reduction of dichloroindophenol and oxidized glutathione.

63. **(Amended)** A method for the prophylaxis or treatment of arteriosclerosis, diabetes, ischemic disorders, edema, vascular hyperpermeability, inflammation, gastric mucosa disorders, acute pancreatitis, Crohn's disease, ulcerative colitis, liver disorders, Paraquat's disease, pulmonary emphysema, chemocarcinogenesis, carcinogenic metastasis, adult respiratory distress syndrome, disseminated intravascular coagulation, cataracts, premature retinopathy, auto-immune diseases, porphyremia, hemolytic diseases, Mediterranean anemia, Parkinson's disease, Alzheimer's disease, epilepsy, ultraviolet radiation disorders, radioactive disorders, frostbite or burns, comprising [the administration] administering to a mammal in need thereof [an] a pharmaceutically effective, non-toxic dose of a peptide [encoded by the polynucleotide sequence of claim 49] which comprises the amino acid sequence consisting essentially of amino acid numbers 1 to 526 of SEQ ID NO: 12, and which catalyzes the reduction of dichloroindophenol and oxidized glutathione.

71. (Amended) An antibody [or an equivalent thereof,] which specifically recognizes KM31-7 protein[, or which specifically recognizes a mutant or variant of KM31-7 protein].

73. (Amended) The antibody of claim 71, wherein said antibody [antigenically resembles a human antibody] is humanized.

77. (Amended) A process for the purification of KM31-7 protein comprising [the use of] contacting the antibody of claim 71 with a suspension containing KM31-7 protein to bind said protein.

80. (Amended) A polypeptide comprising the sequence [given by] consisting essentially of residues 4 to 437 [in sequence] of SEQ ID [number] NO: 2 [, or a mutant or variant thereof].

Attorney Docket No. 950376D1/HG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Tohru TAKAHASHI et al.

Serial No. : (Divisional Appln. of Ser. No. 09/167,151)

Filed : Concomitantly Herewith

For : EXPRESSION SYSTEMS UTILIZING AUTOLYZING FUSION PROTEINS AND A NOVEL REDUCING POLYPEPTIDE

Art Unit :

Examiner :

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Date of Deposit: April 25, 2001
I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

Dorothy DeFrancesco

In the event that this Paper is late filed, and the necessary petition for extension of time is not filed concurrently herewith, please consider this as a Petition for the requisite extension of time, and to the extent not tendered by check attached hereto, authorization to charge the extension fee, or any other fee required in connection with this Paper to Account No. 06-1378.

LETTER TO THE OFFICIAL DRAFTSPERSON

Assistant Commissioner for Patents
Washington, D.C. 20231

S I R :

Fig. 12 was amended to separately label Figs. 12A and 12B. A red inked, marked up copy of Fig. 12 is enclosed.

Submitted herewith are 13 sheets of Formal Drawings containing Figs. 1 to 13. Please substitute the enclosed drawings for Figs. 1 to 13 as originally in the grandparent application Serial No. 08/500,635.

Respectfully submitted,

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Encs.: (1) Formal Drawings for Figs. 1 to 13 (thirteen sheets)
(2) Red inked, marked up copy of Fig. 12

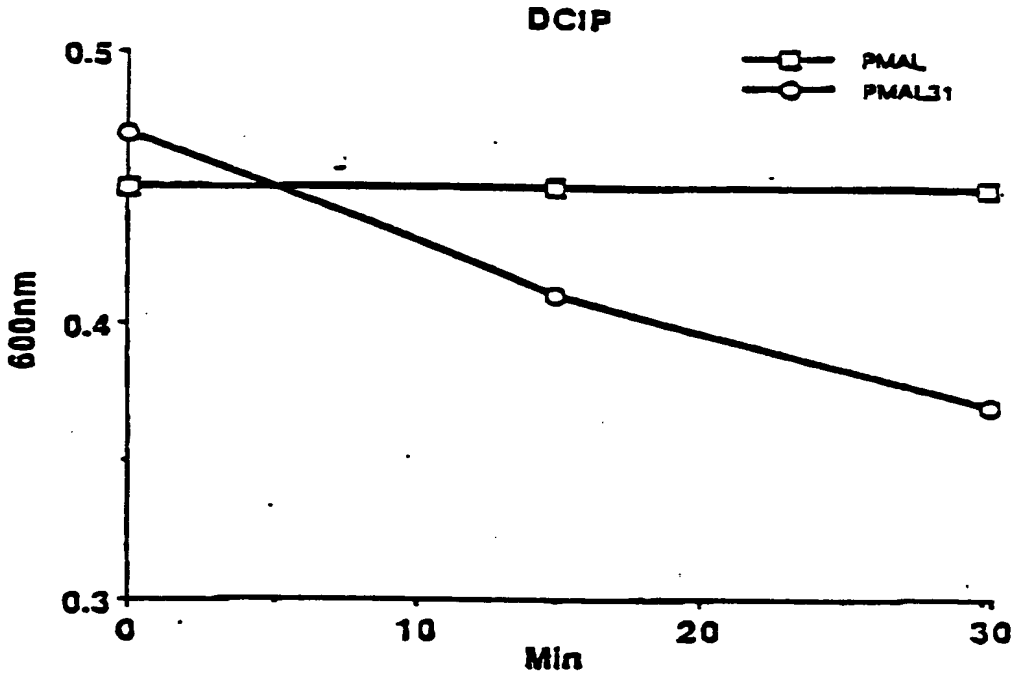

FIG. 12A

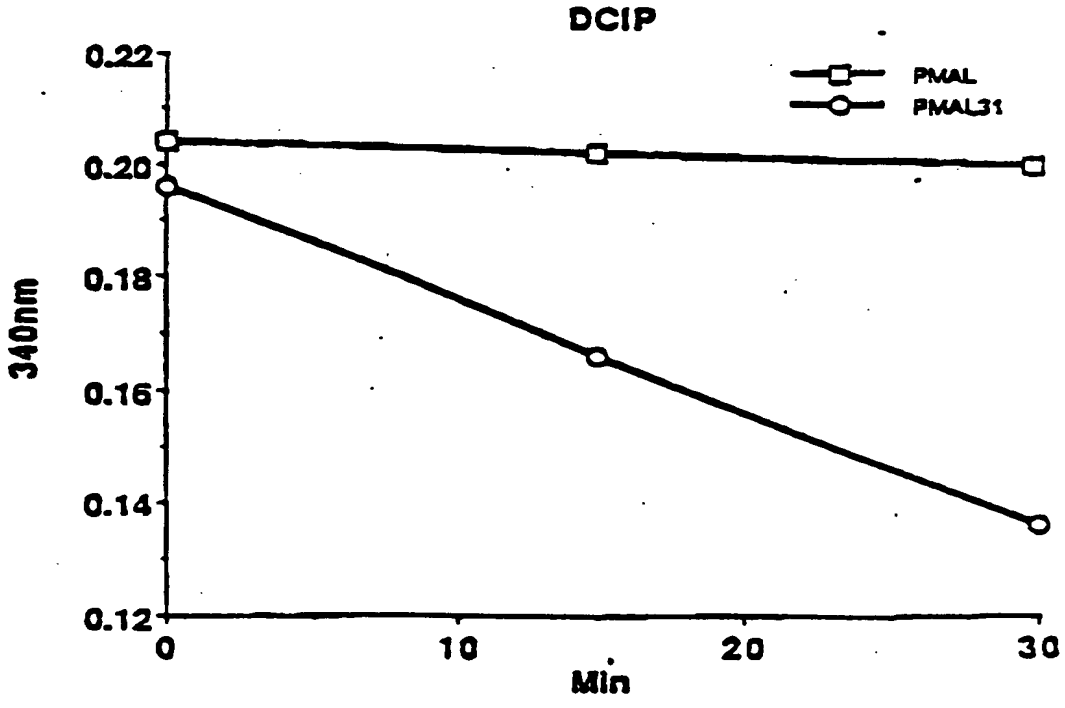

FIGURE 12B